hospitals. The model predicts dyspnea, which is a common side effect of radiotherapy treatment of lung cancer.
Materials/methods: Clinical data from 229 lung cancer patients, treated with curative intent with chemoradiation (CRT) or radiotherapy (RT) alone were collected and stored in 5 different medical institutes (123 patients at Maastro (Netherlands, Dutch), 24 at Jessa (Netherlands, Dutch), 34 at Liege (Belgium, Dutch and French) and 48 at Aachen (Germany, German)). None of the patients received stereotactic body radiotherapy. Patients were treated for their primary lung tumor and had not had another tumor in the 5 years before treatment.
A Bayesian network model was trained on these data. Structure learning was done using the PC-algorithm at each hospital[1]. Network structures were transmitted to the central location, and using a voting algorithm, the optimal network structure was determined. Conditional probability tables were learned using the EM-learning algorithm[2]. Performance of the model was compared for a structure that was learned from multiple hospitals against a structure that was learned locally. The models were trained on data from Aachen, Liege and Jessa and validated on the data at Maastro. Performance was assessed using the area under curve (AUC) of the receiver operator characteristic. ROCs were compared using a method described by DeLong et al [3].
Results: The network structure of the globally learned Bayesian network can be observed in figure 1. The model performed above chance level for making predictions (AUC = 0.69, 95% CI: 0.58-0.80). The model that used a structure originating from local learning also performed above chance level (AUC = 0.67, 95% CI: 0.55-0.79). The globally learned structure allows the Bayesian network to perform marginally better (AUC of 0.69 vs 0.67), however, this improvement is not significant (p = 0.69).
Conclusions: In this work we show that it is possible to train a Bayesian network in a distributed setting, making a big stride forward to enabling personalized medicine in radiotherapy.

Keywords: Dyspnea, Bayesian networks, Distributed learning

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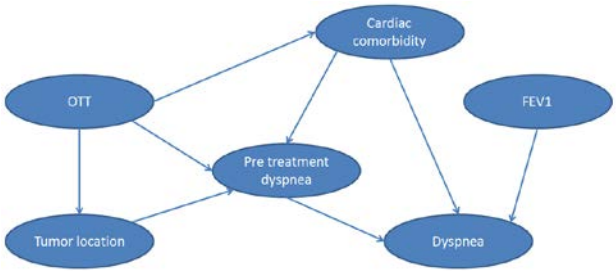

Figure 1: Network structure of the Bayesian network model. The Bayesian network uses, tumor location (right lower lobe, right middle lobe, right hilus, right upper lobe, left lower lobe, left upper lobe, left hilus, mediastinum), FEV1 (forced expiratory volume in 1 second, in %, adjusted for age and gender; measured prior to medication), pre-treatment dyspnea score (CTCAE grade < 2), baseline dyspnea score (CTCAE grade < 2), OTT (overall treatment time) and cardiac comorbidity (Non-hypertension cardiac disorder (at baseline)) to classify acute dyspnea.

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RSI: A genomic signature of radiosensitivity
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Most cancer patients receive radiation therapy (RT) during their illness. Virtually all RT courses are based on techniques and fractionation schemes determined by trial and error, often decades ago. Thus there is a pressing and urgent need for a molecular diagnostic to inform personalized RT delivery. Our team developed a molecular fingerprint of tumor radiosensitivity (RSI), and has subjected it to extensive clinical and analytical validation (1-5). RSI score distribution across disease sites is consistent with their known clinical radio-responsiveness as defined by the surviving fraction after 2 Gy (SF2), and has been validated in 2,200 patients in 12 independent datasets across several disease sites. We have shown that RSI correlates with outcome only in patients treated with RT; it is not prognostic but predictive. The National Cancer Institute designed the Clinical Assay Development Program (CADP) to assist with the development of assays that may predict therapy response or prognostic behavior of a diagnosed cancer; RSI has undergone further development through CADP.
Using RSI and the linear quadratic model, our team next modeled the genomically adjusted dose (GAD) to predict RT dose effect at the individual patient level. RSI/GAD has predicted cancer cohorts that will specifically benefit from RT-dose escalation, such as radioresistant luminal lesions in breast cancer (6) and some glioblastomas (7). Current data have also revealed that metastatic lesions have markedly different RSI than the primary lesion, which is further modified by the site of metastasis (8).
We will discuss current knowledge of RSI/GAD and describe ongoing current research plans to incorporate RSI, as a predictive biomarker of radiosensitivity, into personalized therapy options for RT patients.

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